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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/921,143 | 08/03/2001 | Timothy Coleman | PF112P6 | 6449 |

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| EXAMINER | |
|---|---|
| QIAN, CELINE X | |
| **ART UNIT** | **PAPER NUMBER** |
| 1636 | |

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/921,143 | COLEMAN, TIMOTHY | |
| | Examiner | Art Unit | |
| | Celine X Qian | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *17 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *6-9 and 15-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 10-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *8/3/01* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 6/9/03, 3/12/02, 2/4/2002
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

Claims 1-18 are pending in the application.

### *Election/Restrictions*

Applicant's election with traverse of Group I in the response filed on 12/17/03 is acknowledged. Applicant traverses the restriction requirement for following reasons. First, Applicant requests the clarification of Group I, in which Applicant argues that none of the claims is drawn to an aqueous solution comprising the pVGI.1 vector. Second, Applicant argues that none of the claims in Group III is drawn to an animal comprising the nucleic acid molecule. Third, Applicant argues that the invention of Group II is drawn to a method of using the nucleic acid of Group I in gene therapy, which entails a protein that is produced recombinantly. As such, Applicant concludes that the invention of Groups I and II are not patentably distinct.

This is not found persuasive for following reasons. Claims 2 and 11 encompasses any composition, including a cell, a plant, an animal, or a chair that comprises the nucleic acid. Therefore, in the case where the claims read on a transgenic animal, they are grouped into Group III because it is patentably distinct from the invention of Group I for same reasons set forth in the record mailed on 12/2/03. The invention of Group I is drawn to an isolated nucleic acid, and claims 2 and 10 will be examined in so far as they read on an composition except transgenic animal comprising a nucleic acid molecule, not any plant, animal or anything else comprising said nucleic acid molecule. As for the statement regarding the expression vector pVGI.1 can be used to produce protein recombinantly, the Examiner meant that the vector could be used for *in vitro* production of VEGF2. This is a materially different process of using the vector. Therefore, the invention of Group I and II are patentably distinct.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 6-9 and 15-18 are withdrawn from consideration for being directed to non-elected subject matter. Claims 1-5, 10-14 are currently under examination.

### *Claim Objections*

Applicant is advised that should claim 4 and 13 be found allowable, claim 5 and 14 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. Similarly, should claims 1-5 be found allowable, claims 10-14 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

### *Claim Rejections - 35 USC § 101*

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 2 and 11 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims recites a composition comprising the isolated nucleic acid molecule. The composition read on a human, which is a non-statutory subject matter.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 3, 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

The nature of the invention

The nature of the invention is a method of producing a host cell comprising introducing the pVGI.1 vector into a host cell, and a composition comprising the nucleic acid comprising the pVGI.1 expression vector. The claims read on introducing of the pVGI.1 vector to a host cell in an *in vivo* setting. Consequently, claims 2 and 11 also read on a human comprise a pVGI.1 vector in a cell.

The breadth of the claim

The breadth of the claim is broad. Claims 3 and 12 encompasses a method of producing a host cell comprising the pVGI.1 vector both *in vitro* and *in vivo*. In addition, claims 2 and 11 encompasses any composition that comprises said pVGI.1 expression vector.

The teaching of the specification

The teaching of the specification is limited. The specification teaches that the pVGI.1 expression vector comprises a polynucleotide encoding VEGF2. The specification teaches that this vector can be used in gene therapy for ischemia and coronary artery disease. However, the specification does not teach a method in which this vector is used and achieve a therapeutic effect in gene therapy. Furthermore, the specification fails to provide a working example for using this vector in gene therapy.

The state of art at the time of filing and level of predictability in the art

The state of art at the time of filing considers the success of gene therapy as unpredictable. Verma et al. (1997, Nature, Vol. 389, pages 239-242) and Anderson et al.(1998, Nature, Vol. 392, pages 25-30) discuss the inherent difficulties in gene therapy. The major difficulties include poor delivery systems and poor gene expression after delivery (see Anderson, page 30, 1st col., 5th paragraph). Verma et al. also point out that the problem with the success of gene therapy is inability to delver genes efficiently and to obtain sustained expression (see page 239, 3rd col., 2nd paragraph). In addition, Verma et al. also indicate that another factor that affect the efficacy of gene therapy is the immune system of the host organism (see Verma et al., page 239, 3rd col., last paragraph). The human host immune system fights of virus, thus making the use of viral vectors less efficient. Therefore, in view of the above technical difficulties, one of

skilled in the art would have to rely on the teaching of the specification to practice the method as claimed.

The specification only teaches that pVGI.1 is an expression vector that expresses VEGF2. The specification fails to teach any method that would overcome the art recognized difficulty in using pVGI.1 for gene therapy. Since the claims read on the *in vivo* therapy by introducing the pVGI.1 vector into a human being, and the composition also read on a human comprising said vector in a cell *in vivo*, one of skilled in the art would have to engage in undue experimentation to practice the invention as claimed because the lack of guidance of the specification and art recognized unpredictability. Therefore, the claimed method and composition is not enabled by the instant specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 12 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 1-5, the recitation of "the pVGI.1 expression vector construct depicted in Figure 31" renders the claims indefinite because Figure 31 displays a nucleic acid sequence rather than the construct itself.

Regarding claims 3, 4, 12 and 13, the recitation of "a method of producing a host cell comprising...transfecting a host cell" renders the claims indefinite because it is unclear whether the second host cell is same as the first host cell.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-5 and 10-14 are rejected under 35 U.S.C. 102(a) as being anticipated by Vale et al (Circulation, 1999, Vol.100, No. 18, p.I.22).

The claims are drawn to an isolated nucleic acid molecule comprising the pVGI.1 expression vector, a composition comprising the isolated nucleic acid molecule, a host cell comprising said nucleic acid molecule, and a method of producing said host cell by transforming, transducing or transfecting the nucleic acid molecule.

Vale et al. disclose a pVGI.1 vector that expresses VEGF2 (see abstract). Vale et al. further teach that the vector is directly injected into ischemic myocardium of porcine (see abstract). Therefore, Vale et al. disclose the instantly claimed inventions.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine Qian, Ph.D.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER